

IN THE SPECIFICATION

Please replace the paragraph beginning on page 4, line 8, with the following replacement paragraph:

The results of experiences made by the Inventors, operating with truncated forms of the DEN-2 ectodomain indicate that the nine carboxy-terminal amino acids of the M ectodomain (M32-40) constitute an intrinsic apoptotic sequence. The discovery of M32-40 brings to light a role for the small membrane M protein in DEN virus pathogenicity. Detailed comparison indicated that M32-40 of the four serotypes of DEN where more than 75% identical. Searches on nucleotide and protein databases showed that the nine-residue sequence responsible for the cytotoxic effect of the M ectodomain displayed no obvious similarity with any known cellular protein. Viscerotropic YF virus causes damage to liver cells in humans and hepatocytic apoptosis has been observed in infected livers. Two live attenuated vaccine strains, 17D and French neurotropic virus (FNV) are known to have the ability to cause viscerotropic disease. Comparison of the genomes of the YF vaccine strains 17D and French neurotropic virus (FNV) with the parental and other wild-type YF viruses revealed a common difference at position M36: the isoleucine residue at this position in the wild-type YF virus (Asibi) was replaced by a phenylalanine (17D vaccine strain) during attenuation. The Inventors demonstrate for the first time that the ~~[[L36F]]~~ I36F substitution observed in YF vaccine strains abolishes the death-promoting activity of the YF M ectodomain. The ~~[[L36F]]~~ I36F substitution also results in a reduction of the cytotoxicity of the DEN-2 ectodomain. Thus residue M36 not only plays an essential role for the efficient induction of apoptosis by peptides M32-40 containing it, but also the residue M36 is critical for the attenuation of viscerotropic flaviviruses.